
Preface

Vaccines are currently regaining attention from members of the medical and scientific communities but even the broader public, including heads of state. This level of public awareness of the fundamental relevance of vaccines for global human well-being has been rekindled by dramatic threats of rapidly emerging infectious diseases (predominantly caused by viruses) and increasingly widespread multidrug-resistant bacterial infections. Insect-borne Zika virus and Ebola fever are only the most recent examples demonstrating a persistent vulnerability of human society to such primordial threats. In another area, cancer immunotherapy, vaccines are a promising, innovative treatment modality, too. In future, integrated treatment regimens that include cancer vaccines may enable patients to better regain immunological control over the tumor, superseding or complementing today's immune checkpoint inhibitors.

RNA vaccines, the subject of this volume, span a spectrum from recombinant viruses to self-amplifying mRNA and nonreplicating mRNA vectors. Given this breadth, we firmly believe that RNA technology will eventually spawn vector platforms of enormous medical and commercial potential. All RNA vaccines share distinct features, which will likely contribute to their continuing relevance:

- Like viruses, they provide integrated stimuli to adaptive and innate immunity, i.e., antigen expression *in situ* and danger signaling, e.g., via toll-like receptor pathways.
- Like live vectors, they induce “balanced” immune responses that comprise humoral and cellular effectors as well as immunological memory.
- Synthetic RNA vaccines allow for a combination of different antigens without increasing the complexity of vaccine formulation, thus facilitating speedy and flexible production.
- Due to “vector neutrality” they generally allow for highly repetitive vaccination schedules with consistent boost potential and no or little immune response directed against the vector.
- Thermostable RNA vaccines could simplify transport and stockpiling even in the absence of a cold chain, a frequently underestimated hurdle for global disease control.

In any case, unlocking this potential will require continued optimization as well as informed choice of applications.

Thus, the aim of this volume is to facilitate both efforts by assembling an overview of the field and practical hints for vaccinologists in academia and industry. Different RNA vaccines exhibit diverse sets of trade-offs with respect to efficacy, reactogenicity, and handling that reflect the great versatility of this class of vaccines. To choose the best way ahead, a basic understanding of the regulatory framework, including aspects of nonclinical safety testing and good manufacturing practice, is essential. The scope of protocols included in this book is laid out and discussed in more detail (together with some scientific context and additional references) in the introductory, first chapter. The protocols include relevant pointers to current “best practice” with concrete tips and tricks in the notes section of each chapter.

Finally, we are well aware that the relevant body of knowledge is rapidly developing and cannot realistically be captured in a single volume. We, therefore, sincerely hope that this compendium may engender increased collaboration on RNA vaccines between basic and applied scientists in academia, government, and industry to develop future solutions for today's challenges. In any technological field, we need reliable maps that are drawn from facts and open discourse to safely navigate both hyperbole and pessimism. We hope that this book will offer helpful orientation.

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